

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No. 10/627,452

Customer No. 23379

Applicant: Daniel Portnoy and Darren Higgins

Confirmation No. 3443

Filed: Jul 25, 2003

Group Art Unit: 1636

Docket No. B98-039-4

Examiner: Makar, Kimberly A.

Title: *Intracellular Delivery Vehicles*

## DECLARATION UNDER 37CFR1.132

I, Darren E. Higgins, declare and state as follows:

1. I am an Associate Professor of Microbiology and Molecular Genetics at the Harvard University Medical School. I have authored numerous peer-reviewed publications relating to using microbes to deliver foreign agents to eukaryotic cells. I am an inventor of the subject application, and a co-author of Radford et al. (Gene Therapy 2002, 9, 1455-63) and Bouwer et al. (PNAS 2006, 103, 5102-7).
2. The Specification teaches the introduction of a variety of foreign agents for a variety of purposes (e.g. p.4, line 19 - p.6, line 3), including antigenic and therapeutic agents. The Specification teaches use of a variety of nonvirulent bacteria (e.g. p.6, lines 4-20) and target cells (e.g. p.6, line 21 - p.7, line 12). The specification teaches a variety of effective routes of in vivo and ex vivo administration depending on the nature of the foreign agent (e.g. p.7, line 13 - p.8, line 14). In addition, the specification provides numerous demonstrative examples of the method as applied to numerous foreign therapeutic agents (note that in some embodiments, an antigenic agent will suffice as a therapeutic agent; therapeutic agents include prophylactics such as immunizations, e.g. p.4, lines 21-22) and a variety of target cells in vivo and ex vivo (e.g. p.8, line 15 - p.10, line 11).
3. In my expert opinion, the application provides ample teaching to enable one of ordinary skill in this art to practice the claimed method without undue experimentation. In fact, following the teachings of this disclosure without resorting to any undue experimentation, persons skilled in the art have implemented the claimed method to generate an anti-tumour response and to deliver antigens in vivo (e.g. Radford et al., supra; Bouwer et al., supra).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States

Code and that such willful, false statements may jeopardize the validity of the application and any patent issuing therefrom.

Date: 1-9-07

Darren E. Higgins  
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